REMARKS

Status of the Claims

After entry of the complete listing of the claims provided above, the status of the claims in this application are as follows:

Claims now pending in this application include: Claims 1-20 and 953.

Claims now amended include: None.

Claims now canceled include: Claims 21-40 and 954.

Claims previously canceled include: Claims 41-952.

Claim Cancellations

As indicated above, Applicants have canceled several claims (21-40 and 954) in a sincere effort to place their application in better form for appeal by materially reducing or simplifying the issues for appeal. Furthermore, it is obvious that the cancellation of these claims do not raise new issues that would require further consideration and/or search. It is also obvious that these claim cancellations do not raise the issue of new matter. Finally, the cancellation of claims 21-40 and 954 means that no additional claims are presented by this paper.

Entry of the above claim cancellations is respectfully requested.

It should be noted that with the cancellation of claims 21-40 and 954, the present set of claims (1-20 and 953) are each limited to *inherent universal detection targets (UDTs)*.

Before addressing the two art-based rejections, Applicants and their undersigned attorney acknowledge with thanks the Examiner's indication in the March 2, 2005 Office Action (page 2) that three rejections have been withdrawn (indefiniteness under 35 U.S.C. §112, second paragraph; anticipation under 35

U.S.C. §102(e) by Li (U.S. Patent No. 6,696,256); and obviousness under 35 U.S.C. §103(a) over Li in view of Kool et al. (U.S. Patent No. 6,479,650).

Turning to the first art-based rejection, . . .

The Rejection Under 35 USC §102

Claims 1-4, 7, 9-15, 17-24, 27, 29-35, 37-40 and 953-954 stand rejected under 35 U.S.C. §102(e) as being anticipated by Lizardi et al. (U.S. Patent No. 6,261,782, issued on July 17, 2001). In the March 2, 2005 Office Action (page 3), it is stated:

> Lizardi et at. disclose a composition matter that comprises a library of nucleic acid analytes (See column 4, lines 4-11 and See column 61 to column 62, example 1, and column 63 to 64, example 2) and an array of nucleic acids (See column 4, lines 19-20)
>
> Wherein said library comprises diverse nucleic acid analytes, which comprises
>
> (i) an inherent universal detection target (UDT) or non inherent universal detection target comprising at least one conserved sequence present in the diverse nucleic acid analytes (See column 7, lines 1-7, where when a single restriction enzyme is used, then a conserved sequence is generated, and also see column 50, lines 30-66 where FokI cleavage at the DNA results a conserved sequence GGATG sequence ligated to the adapter-indexer, further see column 12, lines 11-13, where a common identical sequence is present in the adapter-indexer),
>
> (ii) a universal detection element (UDE), said UDE being attached to the UDT, said nucleic acid analytes being hybridized to said array of nucleic acids, and said array of nucleic acid being fixed or immobilized to a solid support (See column 4, tines 1-11, column 15, lines 6-48, column 53, lines 23-36),
>
> wherein said UDE generates a signal indicating the presence or quantity of said diverse nucleic acid analytes by means of said attachment of said UDE to said UDT (See column 17, lines 2-15, column 54, lines 28-34 and column 103, lines 6-9).

Continuing on pages 4-5 in the Office Action:

> With regard to claims 2-3, 13-15, 22-24 and 953-954, Lizardi et al disclose that the nucleic acid samples used in the method are genomic sample, mRNA sample, cDNA sample, nucleic acid libraries, whole cell samples, and tissue samples (See column 8, lines 54-59). Preferred nucleic acid samples used in the method are genomic samples and mIRNA samples (See column 8, lines 62-64). Since the terms, for example, secondary structure, splicing elements used in the claims do not have specific sequence, any sequence used in the method reads on these limitations).
>
> With regard to claims 4, 11, 31, and 35, Lizardi et al. disclose that the detector probes immobilized in an array (See column 4, lines 19-20) are oligonucleotides (See column 14, lines 46-48).
>
> With regard to claims 12 and 32, Lizardi et al. disclose that oligonucleotide probe was covalently attached to the surface of a glass-slide via a poly-ethylene-glycol spacer moiety (See column 63, lines 64-66). The spacer moiety is interpreted as a chemical linker or linkage arm.
>
> With regard to claims 7, 9-10, 27, and 29-30, Lizardi et al. disclose that solid-state substrate for use in probe array can be glass (See column 15, lines 55-67).
>
> With regard to claims 17 and 37, Lizardi et al. disclose that the ligator-detector is detected directly or indirectly in which the pattern of ligator-detectors coupled to different detector probes indicates the nucleic acid analytes in the sample (See column 103, lines 6-9).
>
> With regard to claims 18-21 and 38-40, Lizardi et al. disclose that the labels are fluorescent molecules, enzymes, antibodies and ligands (See column 17, lines 11-15).
>
> With regard to claims 33-34, Lizardi et al. disclose adapter-indexer corresponding to UDT comprises homopolymeric sequence or heteropolymeric sequence (See fig 5, panel C and column 6, lines 2-5).
>
> Based upon the analysis above, the teachings of Lizardi et al. anticipate the limitations of the claims.

The anticipation rejection is respectfully traversed.

As indicated earlier in this paper, with the cancellation of claims 21-40 and 954, the present set of claims (1-20 and 953) are limited to *inherent universal detection targets (UDTs)*. It is believed that the anticipation rejection cannot be

sustained because there is a clear lack of identity in material elements between the present invention and claims which call for *inherent UDTs*, and the cited Lizardi patent which disclose at best a *non-inherent* UDTs termed "tags." A reading of Lizardi et al. shows that they ligate an artificial *non-inherent universal detection target (UDT)* to a library of analytes.

In the March 2, 2005 Office Action (page 3, third paragraph from the bottom), reference is made to "a conserved sequence GGATG." This sequence from Lizardi et al. is not considered to be an inherent UDT because it is simply the sequence coding for a restriction enzyme recognition site. As such, Lizardi's disclosed GGATG site is not a conserved sequence so much as a random sequence that will be located at various sites in a polynucleotide sequence. An understanding of a true inherent UDT is given in Applicants' specification (see, for example, page 43, first paragraph; and page 44, last paragraph).

In view of the lack of material identity between the present claims and Lizardi et al., Applicants respectfully request reconsideration and withdrawal of the anticipation rejection under §102(e).

The Rejection Under 35 USC §103

Claims 5-6, 8, 16, 25-26, 28 and 36 stand rejected under 35 U.S.C §103(a) as being unpatentable over Lizardi et al. (U.S. Patent No. 6,261,782, issued on July 17, 2001) as applied to claims 1-5, 7, 9-15, 17-25, 27, 29-40 and 953-954 above, and further in view of Egholm et al. (U.S. Patent No. 6,451,588, issued on September 17, 2002). In the March 2, 2005 Office Action (pages 6-7), it is stated:

> The teachings of Lizardi are set forth in section *5* above. Lizardi et al. do not disclose modified sugar or phosphate or base moieties, and polyacrylamide used as porous solid support.
>
> With regard to claims 6, and 26, Egholm et al. disclose nucleic acid analog through modifications of the sugar and the nucleobase

(See column 4, lines 59-67 and column *5*, lines 26-35).

With regard to claims 5,16, 25 and 36, Egholm et al. disclose high-affinity nucleic acid analog which includes PNA (See column 5, lines 26-30).

With regard to claims 8 and 28, Egholm et al. disclose that the solid support immobilized the probes may be polyacrylamide (See column 15, lines 43-50).

One of ordinary skill in the art would have been motivated to apply the modification to the sugar, or base of the nucleic acid probe in the array of Lizardi et al. The motivation is that the nucleic acid analog as taught by Egholm et at. attains desired properties, for example, optimized hybridization specificity or affinity, chemical stability (See column 4, lines 67 to column *5*, line 1-9) and higher affinity for a strand of DNA than the corresponding complementary strand of DNA (See column 5, lines 26-30). In addition, the method of Egholm et al. for hybridization of a collection of probes to a target nucleic acid is an improvement of nucleic acid analysis in an array (See column 1, lines 59-61 and column 16 lines 1-22) in that the detection can be accomplished following gel electrophoresis (See column 15, lines 61-67. Thus it would have been prima facie obvious to apply the modification to the sugar, or the base and solid support made from polyacrylamide to make the composition comprising the library of analytes, and array of nucleic acid fixed on a solid support and the analytes comprise UDT and UDE.

The obviousness rejection is respectfully traversed.

Applicants incorporate their comments with respect to Lizardi et al. in the above anticipation rejection. It should be pointed that in common with Lizardi et al., the secondary reference, Egholm et al., likewise uses *non-inherent UDTs* for signal generation. In neither cited document, Lizardi et al. or Egholm et al., is there any disclosure or suggestion that *inherent UDTs* could or should be used for signal generation in a library of analytes, as provided by the present invention. Thus, a person of ordinary skill in the art would not have arrived at the present invention from a combined reading of Lizardi et al. and Egholm et al., neither of whom discloses or suggests the use of *inherent UDTs*.

In light of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection under 35 U.S.C. §103(a).

Information Disclosure Statement

Applicants acknowledge the comment on page 7 in the March 2, 2005 Office Action that the references 0104620 and 0104460 lined through in PTO-1449 filed 1/7/04 were not found in the response. Applicants' attorney will submit both documents as soon as possible in a supplemental filing to this paper.

Favorable action on this application is respectfully requested.

* * * * * * *

SUMMARY AND CONCLUSIONS

A complete listing of the claims in this application are provided above. In the complete listing of the claims, 21-40 and 954 have been canceled.

No fee or fees are believed due for this paper, apart from the Request For Extension Of Time (3 Months) and authorization for the small entity fee therefor. In the event that any other fee or fees are due, however, authorization is hereby given to charge the amount of any such fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Early and favorable action is respectfully requested.

Respectfully submitted,

Ronald C. Fedus
Registration No. 32,567
Attorney for Applicants

ENZO LIFE SCIENCES, INC.
c/o Enzo Biochem, Inc.
527 Madison Avenue (9th Fl.)
New York, New York 10022
Telephone (212) 583-0100
Fax (212) 583-0116